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Contents

Editorials

- 4 Let's Talk About It!

News

- 5 Food & Nutrition
Yet Another Blessing From the Blessed Tree.
- 5 Biotechnology
New Prospects for an Old Continent.
- 5 Therapeutics
WW2 Battle Tactics to Save the BirdFlu Drug.
- 5 Physiology
Is Telling the Truth a Gut Instinct?
- 6 Nanotechnology
What Limits Technology?
- 6 Physics
The Beauty of the Answer is Part of its Proof.
- 6 Computing
Linux Everywhere.

Previews & Views

- 8 Java - it it the Technology Standard?
- 8 The Sultan of Swing - The Pendulum.
- 8 In Search of Evidence: Promise and Uncertainty.
- 9 An Introducton to Tissue Engineering.

Letters & Feedback

- 10 On-Chip Optical Interconnect Fabric.
- 11 Cox-2 Selective Inhibitors: The Other Side of the Coin.
- 12 Evolution, Naturalism and Islam.

Biographies

- 28 Ibn Sina, The Prince of Medicine.

Wiewpoint

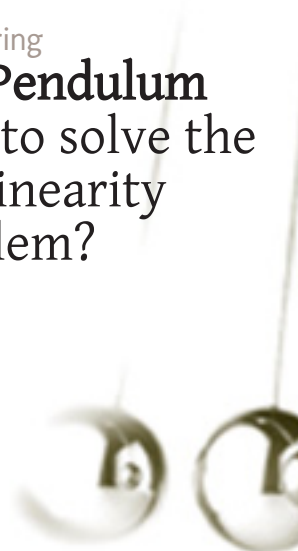
- 31 Why not publish?

Features

- 16 Engineering
The Pendulum
How to solve the Nonlinearity Problem?

Articles & Reports

- 14 Computing
Java Everywhere - Java for Wireless Devices.
- 20 Science
Clinical Trials in Drug Development: An Introduction.
- 23 Science
Tissue Engineering: How Will Surface Engineering Prosper its Applications?



Let's Talk About It!

Leaving aside political correctness, many of you may have heard that "lemon juice may help beat AIDS, measles vaccine may be responsible for autism, genetically modified crops are likely to create super-weeds, and mobile phones can cut male fertility by a third". Such dubious claims are widely communicated to the public and possibly even to the scientific community through the sensationalist press and the peculiar world of online science and medicine reporting. This leaves scientists with a major challenge when trying to convey a message either to the public or their peers.

When it comes to communicating and discussing scientific matters and even other matters, polarisation, oversimplification and exaggeration present a huge obstacle resulting in an inevitable failure of the whole process. This is simply because oversimplification and polarisation tend to represent many public choices as false dichotomous facts.

With this in mind and due to the huge popularity of Internet forums nowadays in scientific circles, IBScientific, in addition to its publication, has taken advantage to establish a domain that enables free-exchange of opinions and ideas among frequent and infrequent members through an interactive web forum. IBScientific forum aims primarily to enhance academic communication and discussion as well as to promote both disseminating and seeking knowledge. Regarding communication, IBScientific forum allows members to ask direct questions that require straight forward answers, it also allows conducting surveys and questionnaires, again in a direct manner. Discussion through the forum on the other

hand, is manifested in debates and dialogues to enrich ideas and opinions.

Last but not least promoting knowledge is a fundamental aim of IBScientific and its forum. Promoting knowledge through the forum could be achieved by single members teaching and learning by writing in a particular matter with continuous update. This process does not necessarily require interactive communication or discussion. Promoting knowledge through the forum has to be particularly emphasised, as it seems to be the least popular aspect within this interactive domain. The reasons for this, I must argue, lies in the lack of interactions between the contributors to the topic making it somehow unattractive, nonetheless still very important.

I guess the message I am trying to convey here is that we can, in IBScientific Forum, communicate and debate; and we can teach and learn.

So let us talk on it and let's talk about it... ■

Abderrahmane KAIDI
IBScientific Board

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Food & Nutrition

Yet Another Blessing From the Blessed Tree



APART from being a delicious component in the Mediterranean diet, extra-virgin olive oil contains a compound that may give some long-term health benefits including reduced risk of cancer and Alzheimer's mimicking ibuprofen effects. A team led by Paul Breslin of the Monell Chemical Senses Institute in Philadelphia has reported in *Nature* [1] that the compound oleocanthal, despite having a completely different chemical structure, acts similarly to ibuprofen to inhibit some components of the prostaglandin pathway important for pain signaling in humans. Despite the fact that any extra-virgin olive oil should contain oleocanthal, Breslin emphasizes that most supermarket's extra-virgin olive oils may be relatively low in this compound. The good news however, is that there are inexpensive olive oils that contain high levels, and here he explains how to test for it: "The way to check is

to sip the oil neat and see how strongly it stings the throat," Breslin recommends. He continues explaining: "The greater the sting the greater the oleocanthal level." This probably puts the famous Algerian olive oil amongst the healthiest in the world.

Y.M. Source: *Nature*

Biotechnology

An African Panel for Biotech: New Prospects for an Old Continent

A new panel, co-chaired by Ismail Seragudin, a former executive with the World Bank, and Calestous Juma, a former executive secretary of the UN Convention on Biodiversity, was recently established to investigate what is needed for a home-grown biotech industry in African countries. Juma told *SciDevNet* [2] that some significant research has already started in a number of countries such as East Africa on agriculture, in Egypt and South Africa on biomedical research and in Nigeria in various fields. He sees that the current challenge is in making biotech relevant to local needs and in ensuring good cooperation from the existing institutions. However testing and distributing biotech products is particularly problematic in Africa, where biotechs are generally viewed as troublesome. For example, several months ago, Foster City, California-based Gilead Sciences, was forced to cancel clinical trials of its AIDS drug Viread (tenofovir) in Kenya, South Africa and Cameroon after charges from activists

opposing the trials for being a form of exploitation. The newly released film, *The Constant Gardener*, based on John le Carré's 2001 novel about an evil drug company attempt to market its drug for tuberculosis in inhumane ways, reflects this negative view.

Nevertheless, this is not the main problem as Lawrence Kent, director of international programs at the not-for-profit Donald Danforth Plant Science Center in St. Louis, says. She believes that the main difficulty is in persuading government officials throughout Africa to the need of biotech and the regulations and funding incentives required to nurture and sustain startups.

Y.M. Source: *SciDev.Net*

Therapeutics

WW2 Battle Tactics to Save the Bird-Flu Drug



A recent breakthrough has been made to effectively double supplies of Tamiflu, the main medicine recommended by the World Health Organization (WHO) to fight bird flu. Administering Tamiflu alongside a second drug stops it being excreted in urine, meaning that only half doses of the treatment would be needed. Earlier, the WHO had recommended countries worldwide to stockpile enough drug for at least 25% of their population, in a preventive action against an eventual flu pandemic. Although Swiss drugmaker Roche, the sole supplier, has quadrupled its production

capacity over the past two years, the current supply is thought to cover only 2% of the world population. Last November, Jowe Howton, medical director at the Adventist Medical Center in Portland, Oregon, found that in an earlier work published by Roche [3], giving the flu drug together with a simple benzoic acid derivative, probenecid, doubles the time that Tamiflu's active ingredient (oseltamivir phosphate) stays in the blood, and multiplies 2.5-fold the patient's total exposure to the drug. Notably, this technique was first used during the Second World War to stop many drugs, including antibiotics, being removed from the blood by the kidneys. Roche who published the probenecid data in 2002 claim that there are insufficient data while many doctors argue that the drug combination to be used safely, even without specific approval from regulatory agencies.

Y.M. Source: *Nature*

Physiology

Is Telling the Truth a Gut Instinct?

IS telling the truth a gut instinct? Researchers report 31 October 2005 at the annual meeting of the American College of Gastroenterology that electrical rhythm of the stomach undergo significant changes when a person is saying a lie. They used an electrogastrogram, a device similar to an electrocardiogram but that has electrodes which are put over the belly rather than the chest. Lie detection tests can benefit greatly from this device, especially that some subjects can fool standard polygraph tests by regulating their breathing.

Y.M. Source: *Science News*

This issue's news were collected by:

Y.M. Younes MOKRAB
A.B. Abdeldjalil BENNECER
A.M. Ahmed MAACHE

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Nanotechnology

What Limits Technology?

Although the news coverage on Nanotechnology is reported to be scarce [4], scientists, technologists and government officials endorse it as the next revolution. why?

Nanotechnology uses the bottom-top approach, mimicking living organisms to self-assemble infinitely small scale units, by carefully positioning atoms with great precision to fabricate the desired device. That is why the American federal government is spending \$1 billion this year in addition to an endless stream of money coming from corporations and investors worldwide towards nanotechnology research (\$4 billion to date).

Professor C. Lieber and his colleagues in the Harvard's Department of Chemistry and Chemical Biology and the Division of Engineering and Applied Sciences [5] have fabricated 10 nanometre (50 atoms) detector devices for viruses and diagnosis of prostate cancer markers. The endeavour towards miniaturisation is not only targeting small and efficient devices, but also creating tools that enable making the increasingly small nanoproductions. The same group has published in the 25 November issue of Science an article about new ways of constructing devices. The work consists of making devices right into wires along with their information and function instead of fabricating wires to connect different parts of devices that are later programmed to perform a certain function and contain some information.

The developed technique came as a breakthrough because it is not only cheaper compared to lithography but also more efficient. In addition, lithography is limited by spaces on the patterns of the circuit which in turn limits the number of devices and switches on any chip. As this spacing is getting smaller, the temperature and electric fields generated will hinder

the operation of the device.

Professor Lieber and his colleagues have announced that they have pushed the limits even further by solving such problems that were unreachable with conventional lithography. With this method, it is possible to construct switches and amplifiers by having nano-wires in vacuum reactor in which different gases precisely flow onto defined sections. These gases are responsible for doping the silicon with impurities to change the conductivity switching electricity and light, amplifying them or just changing them in some way.

The future of nanotechnology is promising and a myriad of application is already making its way through from laboratories as a proof of concept but may be very soon, real potential devices [6].

A.B. Source: PhysicsOrg.com

Physics

The Beauty of the Answer is Part of its Proof

AS if physicists are not convinced yet about what is probably the most famous formula in science, $E=mc^2$, physicists from the Massachusetts Institute of Technology (MIT) and the Commerce Department's National Institute of Standards and Technology (NIST) have reported the most precise direct test of Einstein formula which describes the relation between matter and energy.

The paper published in Nature 21/12/2005 [7] offers a further improvement to the precision of measurements reported hitherto to confirm the theory of special relativity by an order of 55 folds according to the paper.

Scientists from NIST found 0.0000004 difference in their calculation of energy emitted from silicon and sulfur atoms compared to the result from their colleagues in MIT of the

mass of the same atoms.

The novelty of this work comes not only as additional precision but also as direct test to the theory. Previously, better approximations have been reported but it often required some assumptions to explain, which in some cases makes the result awkward to interpret. There are two different methods developed by the two groups one using optical and X-ray interferometry to determine with great accuracy the spacing between atoms and the other one using the calibrated crystals to measure the short wavelength characteristics.

The team from NIST detected the gamma rays emitted from Silicon and Sulfur atoms and according to photoelectric relation, that Einstein had the biggest stake in its interpretation, energy and wavelength are related by the Planck's constant. This means by measuring the wavelength, it is possible to deduce the energy contained within.

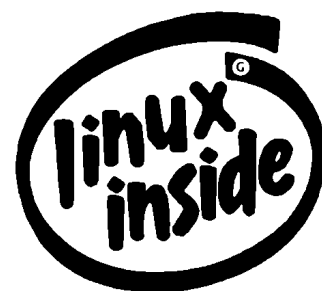
Using a small electromagnetic trap, the MIT team placed two ions, one with an extra neutron, to calculate the mass numbers. This novel technique is immune to many noise sources as it uses the difference between frequencies made by each ion in the magnetic field.

Both methods described above are based on the energy released as gamma radiation when an atom captures a neutron. The theory of special relativity is of prime importance to many physical concepts as well to instruments such

Global Positioning System (GPS), tests of this kind are even useful to other physical experiments.

A.B. Source: PhysOrg 21/12/2005

Computing



Linux Everywhere

"Linux is coming to a consumer electronics device near you soon, thanks to Texas Instruments' (TI) new DaVinci chip".

The new DaVinci digital signal processing (DSP) from Texas Instruments (TI) is now shipped together with MontaVista Linux. This product could encourage other companies to bring Linux into hundreds of millions of devices, as this market is expected to grow continuously in the future.

DaVinci represent TI's next era of digital video solution for consumer electronics. It is an integrated environment that offers development tools and optimized applications in addition to the MontaVista Linux Professional Edition OS. This move will ease the devel-

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opment of digital video products and bring costs down by using an open system.

Huy Pham, DSP System-on-Chip product marketing manager at TI, told *internetnews.com*: "What [DaVinci] does in partnership with MontaVista is enables the Linux developer to use the DSP without needing to understand the complexity of programming the DSP."

DaVinci integration was a result of the partnership of TI and MontaVista for the past 18 months. DaVinci is not the only TI chip that supports this distribution of Linux; however, it is the only chip that put Linux as a key part of the overall system.

TI's decision to incorporate MontaVista Linux is because of its hard real-time capabilities for the kernel. "Pham noted that the response time of the latest MontaVista Linux is 'tremendous'".

The Linux operating system offers TI and its electronics consumers an open platform making software development easier with more cost-effective solution. However, the use of Linux presents legal challenges as the kernel is licensed under the GPL which could oblige firmware vendors to open their own source code for public use. TI is providing some legal advice to its consumers to avoid such issues by separating GPL and non-GPL code. This issue will not prevent TI from working with MontaVista Linux, Pham explained "Our customers so far have all expressed interest in working with MontaVista Linux instead of a roll your own approach because they understand the support that MontaVista provides both on the technical side and on the legal side,".

A.M. Source: *Internetnews.com*
05/12/2005

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Java – is it the Technology Standard?

Review By:
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JAVA software runs on more types of consumer and embedded devices, smart cards, ATMs, thin clients, PCs, servers, and mainframes than any other software. According to Sun Microsystems, "The Java economy includes 750 million Java Cards, 650 million PCs shipped with Java, 579 million Java Powered phones, and 100 telecommunications carriers who deploy Java technology" and if you are looking for something compatible, secure and fast to develop; Java is usually the right choice.

No wonder! A. Maache [1] discusses the roadmap for embedded software in wireless devices and proposes Java as the most adopted and used language. Before he delves into the virtues of Java, he commences by outlining the resource and power limitations experienced by developers for embedded space. The author, then, advises that Java is the way forward and supports his arguments with advantages of this language like portability and the useful built-in functions and libraries which provide a robust and an easy development platform. Ahmed Maache, in his article, does not dismiss the main disadvantage of the well endorsed language in being slow to execute compared to C/C++ and the amount of memory it occupies. Companies and technologists also share his view and agree to embrace Java as the language for embedded systems. The author illustrates with examples the development environments already existing in the market for this purpose, and talks about their characteristics and features.

The author uses the phrase "carefully written software" to indicate the extent of the problem with embedded systems and suggests Java as a solution because it hides many difficulties developers may face. To conclude, Ahmed Maache summarizes the benefits of using the Java 2 Platform, Micro Edition (J2ME) and recommends it for any developer needing to write a piece of software for wireless devices.

The Sultan of Swing – The Pendulum

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AMIDST the splendours of the nonlinear dynamics and chaos temple, D. Rezgui [2] invites us to enter a dancing ball where the pendulum is the sultan of swing; a journey to the unpredictable with the simplest dynamical system in its motion, yet very subtle and intriguing in its behaviour. The synchronous rhythm of the pendulum seems its inexorable destiny based on the analysis of the simplistic ideal mathematical model. Although the author does not set aside this naïve approach to solve any dynamical system state equations for science to advance, he does not lack the audacity to delve into explaining the laws governing the pendulum dance.

The article is presented for the reader to wonder; each pause is an inspiration for a question in the dynamics of the pendu-

lum. The first swing lesson begins by the usual polite introduction into the definition of the dynamical systems. Then, the swing takes us to the classical description and fundamental assumptions of an imaginary ideal pendulum, for instance, friction free, weightless rigid rod and small oscillations. After that, the author reflects on the assumptions made and embarks on another swing, only this time; the pendulum is allowed to swing with large angles. Despite the existence of classical answers to the system state equations, Rezgui presents us with a simple and powerful geometric method to beautifully depict the dynamics of the pendulum known as the phase portrait. Finally, the author reiterates on the initial fundamental question: Does phase portrait method solve the pendulum equations? Obviously, this approach provides no time dependence essential to understand the nonlinear dynamics.

Acknowledging the swing of the pendulum is nonlinear and chaotic and inherently complex to analyse, now Mr. Rezgui, will the pendulum come to a rest?

In search of evidence: Promise and Uncertainty

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TRADITIONALLY clinical practice was based on contemporary understanding of basic mechanisms of disease. Today, it is mainly driven by Evidence Based Medicine. Clinical trials are used to test new drugs and therapies on human volunteers, a process that for many years has been a path across a minefield. In this issue of IBScientific, Mehellou [3] introduces clinical trials and their use during drug development.

The author hails clinical trials as the backbone of evidence based medicine and defines them as the most reliable source of testing drug safety and efficacy. He then traces their evolution through time from an informal test of plant extracts effectiveness in 150BC to contemporary structured processes with the purpose of

treatment, prevention, diagnostic or quality of life improvement. Each of these four types is defined and explained with examples enforcing their roles in clinical healthcare.

Clinical trials designed to test drugs through different stages or phases are the main focus of the article. At each stage of these trials, a different population of patients is recruited to the trials and therapeutic pros and cons of the drug are evaluated. The author explains in details that these phases sequentially generate an ever detailed profile for the drug in question, and this profile is then evaluated by the responsible body to licence the drug for public usage. First, the drug behaviour in the body is tested on a small number of patients, followed by tests providing evidence for its therapeutic potential and the possible side effects. In later phases, the trial strategy is altered, and the number of patients is increased to allow robust statistical analysis giving the drug's safety and efficacy the seal of approval. Though granting the licence, another trial may be conducted mainly for marketing purposes.

In this journey, Mr Mehellou shed light on the importance of clinical trials, and the way they are conducted. He has writ-

Articles

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ten this article as an introduction to other aspects of drug development (e.g. drug pharmacokinetics and pharmacodynamics) that he will discuss in the coming issues of IBScientific.

If you are to learn anything from this article, then you will learn humans treasure their well being very dearly.

But, then you are definitely going to learn much more...

An Introduction to Tissue Engineering

Review By:
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TISSUE transplantation is sometimes the only way to cure a disease, but the shortage of donors still remains the limiting factor. This niche has pushed scientists working on different disciplines to join forces and artificially produce tissues.

Tissue engineering aspire to move from bioengineered products, already used in the clinic such as artificial hip joint, to living tissues reconstructed in the laboratory with the aid of biodegradable scaffolds. With such an objective, the choice of scaffold design, fabrication, physical, chemical and mechanical properties is essential for tissue reconstruction. In this issue of IBScientific, Meftah [4] introduces the approach of tissue engineering using synthetic biodegradable polymers. Synthetic biodegradable polymers are



extensively used in the production of scaffolds and despite being advantageous; the optimisation of these polymers into ideal scaffolds is still problematic in many ways. One example is the properties of the scaffold surface, which have been addressed in the article. Various surface engineering techniques are being used and much more are being investigated. The conventional method is to coat the scaffold surface (poly-lactic acid (PLA)

scaffold) with extracellular matrix (ECM) proteins such as collagen. It is an easy method and produces a surface for cellular attachment similar to the in vivo environment of the cells. Other techniques can be used to promote cell adhesion when ECM proteins fail. However, some applications involve the design of scaffold with surfaces that reduce cell adhesion. Surface physical interpenetrating network (SPIN) technique, for example, can be used to incorporate poly (ethylene glycol) (PEG) polymer chains on the surface of PLA scaffolds. PEG is hydrophobic and reduces cell adhesion, hence the suitability of the engineered tissue to further downstream application.

In all, this article gives us a glimpse into the challenges facing mimicking nature and how to improve our understanding of the obstacles facing the new technologies developed. The author has tried to struck a balance in reporting the technical side of tissue engineering and its application. A hard task by any measure, and will make us change how we perceive new technologies and understand the importance of research and development in such new and fascinating areas.

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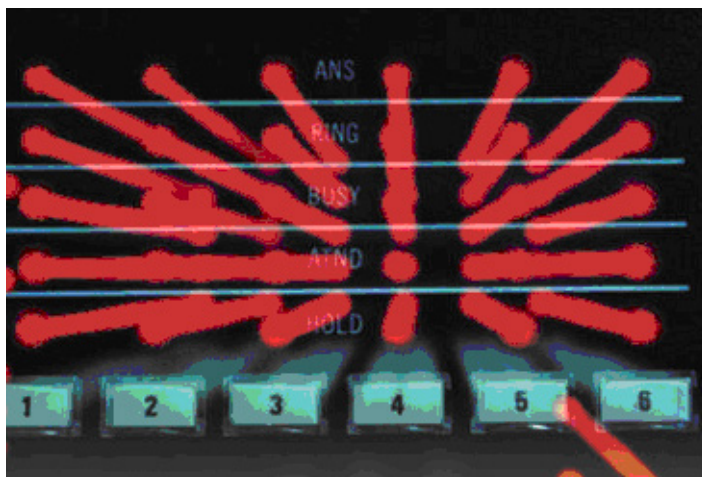
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On-Chip Optical Interconnect Fabric

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Moore's law predicts that the number of transistors per Integrated Circuit (IC) would double every two years. It is then generally realised that this exponential growth will hit a limit in the future. Mammeri (Mammeri, 2005) highlighted that these limits are not due to the increasing integration of semiconductor chips but rather from the interconnections or wire delays increase compared to gate delays. Projections for silicon technology show that the chip size will scale up slightly while the gate area dimensions continue to decrease (Benini and Micheli, 2002; Saraswat and Mohammadi, 1982). The author has put a particular emphasis on the current state of IC technology limitations and then proposed a further motivation by considering network algorithms with respect to interconnections. In this letter, I would like to address the fundamental question on what optics has to offer to solve the interconnect and communication problem.

To my knowledge, there has been no successful implementation of optical logic gates that is at least comparable to their electronic counterparts in terms of speed, density and efficiency. Very little advancements optics has been brought to this research area using several parallel nonlinear elements. Recently, a new European project MUFINS (<http://mufins.cti.gr/>) has been launched to address the All-Optical processing challenge and develop integrated arrays of switches. It is worth, however, noticing that the very difficulty (it is difficult to make photon streams interact) of optics causes in constructing such devices; is exactly the desired property to realise inter-connect technology. Nevertheless, the unqualified successes achieved in fiberoptics on a macroscopic scale offers another encouragement to adopt this solution. The optical layer could increase the bandwidth, decrease interconnect delays, provides immunity to electromagnetic interference and temperature variations, and decrease power consumption.

Given the above facts, it is natural to assume that intrachip optical inter-connect has the potential to outperform electrical wire but there are still challenges and critical hurdles that need to be overcome. At present, there is no clear reference for optical

components parameters apart from International Technology Roadmap for Semiconductors (ITRS) predictions (<http://public.itrs.net/>) which is used to take electrical inter-connect performance as a yardstick for optical interconnect requirements. Considerable efforts have been devoted to realising such a quest including light sources (or lasers), waveguides, modulators, detectors . . . etc. A group from INTEL is already making significant progress in this field reducing the limitations of metal interconnect (Kobrin-sky et al., 2004).

In a comparative study (Haurylau et al., 2005), a group from Rochester University has assessed key parameters of optical vs VLSI interconnects. The first shortcoming is the fabrication processes available to optics. Secondly, this is more of a consequence, there is no efficient monolithically integrated laser (or light source) that could make this dream a reality. One of the solution is to use an external laser source linked to an electro-optical modulator. Suitable Optical waveguide and photo-detectors are readily available to achieve their required task in VLSI. Optical Waveguides already offer a smaller propagation delay and Wavelength Division Multiplexing (WDM) enhances the bandwidth density. This analysis has resulted in defining the requirements for any state-of-the-art modulator to be considered.

There are many other considerations inherent to the optical technology that have not been discussed here and until any progress is made with regards to current issues there is no rational of arising these issues now. While optics still lags behind in VLSI systems, electronics does not look promising either but nonetheless it has a long way to go.

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COX-2 Selective Inhibitors: The Other Side of The Coin

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Sir,

The subject of cyclooxygenase 2 (COX-2) selective inhibitors has recently hit the headlines of the scientific and the public media. Well I guess one could say that VIOXX® (rofecoxib) has become the celebrity drug making the giant pharmaceutical company Merck (the company that introduced VIOXX®) the subject of public sensationalist gossip, formal institutional criticism and most seriously legal battles with the victims' families. This all came about when Merck announced voluntary the worldwide withdrawal of VIOXX® on 20th September 2004 (<http://www.vioxx.com>), as a result of a report revealing increased relative risk for confirmed cardiovascular events, such as heart attacks and strokes, beginning 18 months after treatment of patients with VIOXX® (Topol, 2004). In his article, in the last issue of IBScientific, Mehellou torched on the story of COX-2 selective inhibitors and he noted the long-lived hope but also the more recent hype of COX-2 selective inhibitors (mehellou, 2005).

Here I just wanted to flip the coin, and briefly tell the story of COX-2 and COX-2 selective inhibitors in a slightly different context. Mehello's article focused on the role of COX-2 in inflammatory diseases and the use of COX-2 selective inhibitors as anti-inflammatory agents; here I would like to describe the role of COX-2 in cancer development. It is important to note that COX-2 is not detected in most normal tissues but is aberrantly expressed in tumours of different origins. In the case of colon cancer, for example, COX-2 is abnormally expressed in most adenocarcinomas (malignant/late tumours) and a subset of adenomas (benign/early adenomas). Compelling evidence has accumulated over the years to support the notion that COX-2 contributes to cancer development in different tissues. Whereas COX-2 activation seems to promote colon tumorigenesis in animal models (Oshima et al., 1996), in the breast, however, COX-2 overexpression can even initiate the tumorigenesis process and induce tumour development in an oncogenic fashion (Liu et al., 2001). Abrogation of COX-2 resulted in decreased tumour burden in animal models of human cancer. This suggested COX-2 selective inhibition as a rational strategy for potential chemopreventive and chemotherapeutic intervention in cancer (Elder and Paraskeva, 1998). Indeed, celecoxib (Celebrex®), a COX-2 selective inhibitor that is still available on the market, has been shown to reduce the number of colorectal polyps in familial adenomatous polyposis (FAP) (an inherited form of colon cancer) patients (Steinbach et al., 2000). This potentiated the usefulness of COX-2 selective inhibitors in prevention/therapy of colon cancer especially in the high-risk population, and prompted conducting more clinical trials using other COX-2 selective inhibitors. Indeed, the APPROVe (adenomatous polyp prevention on VIOXX®) trial started in 2003 to assess the effectiveness of VIOXX® as a chemopreventive agent for colon cancer. However, soon after the side effect of VIOXX® were reported (Bresalier et al., 2005) and VIOXX® was withdrawn from the market.

The lessons from VIOXX® story need to be learned by Pharmacia and obviously, for scientists more work is required from them in this area of research. Nevertheless, one needs to emphasise that

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hope and hype are integral part in the application of scientific knowledge in medicine.

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Evolution, Naturalism and Islam

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In his famous book, the selfish gene, Richard Dawkins stated: "Today the theory of evolution is about as much open to doubt as the theory that the earth goes around the sun" (R. Dawkins, 1976). However, by carefully looking at evolution hypotheses and comparing it with the empirical data available today, one rather realizes that Darwinian theory actually open to doubt as much as the theory of the sun orbiting the earth. In addition, interpreting those data in reasonable and logical way rather than constructing imaginative stories from them as done by champions of evolutionist (W.S. Harris and J. Clavart), points to the fact that there is intelligent designer behind such diverse and irreducibly complex biological systems. So what makes Evolutionist hold such a firm belief about the origins of life? Is it really a matter of scientific method or nothing more than a religious belief?

In its fundamental form, evolution theory suggests that all the living organisms existing today originated from a single cell. Simple living organisms evolved to more complex biological systems over millions of years, through two mechanisms:

1. Natural selection which implies that organisms evolve to more advanced species by acquiring new traits in order to survive.

2. The transformation to new specie occurs as a result of random mutations in genes, which itself define the specie. This is entirely random, unguided and mindless process.

In the one hand, natural selection states that the new species are more advanced than the previous ones. If we consider the case between any two species living today which descends from each other, and let's take the human being and the supposed ancestors which for the sake of argument we call primates. Then species which comes in between are more advanced than the primates and less advanced than the human. How come then the primates survived and the species which come as intermediate links extinct although they are the more advanced in the ladder of evolution?!!!

In the other hand, if the process of evolution is entirely random, then there should be many cases where this randomness results in deformed or abnormal shapes of species, and if we discover such deformed species it would be the strongest evidence that evolution really happened. However all the current species and all fossil records show how perfectly and beautifully designed are all the living organisms that ever existed.

It is obvious from these two arguments that the hypothesis of evolution contradicts itself in its logical construct as well as conflicts with all the observed facts. However the question that poses itself; what is going on in the scientific circles nowadays?

The answer to this lies in the concept of naturalism, which is in its essence a belief that all natural phenomena, even emotions, consciousness and thoughts can be reduced to matter and energy and that only physical causes operate (W.S. Harris and J. Clavart). In addition, it rejects the idea of intelligent designer and considers the hypothesis of God and design invalid as a matter of principle and belief, not as a deduction from evidence (W.S. Harris and J. Clavart). Moreover, this belief is considered by many scientists to be a part of the scientific method and not philosophical or religious doctrine. So if we hold such philosophical or rather religious belief, then the evolution theory becomes the only valid explanation for the existence of living organisms.

By contrast Islam as religion asks its followers to first observe natural phenomena and use logic which leads to the deduction that such biodiversity is the fabric of intelligent designer.

I wonder now who is being religious in answering the question of where do we come from. The naturalistic evolutionists who starts first by rejecting design hypothesis and then uses observation and logical reasoning, or Islam which teaches first to use the observation and logic without any prior beliefs in seeking the truth?

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The high demand for embedded computing products including: mobile phones, pagers, personal digital assistants and vehicle telematics systems with sophisticated capabilities like wireless networking, 3G, image and video, increases the need for an application environment that specifically addresses this space. In comparison to the system's resources of a desktop computer, these devices are constrained because their resources are far less than devices developers normally target with desktop applications. This article discusses the considerations that are taken when designing mobile applications, and presents some technologies used in the development of mobile applications.

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Java Everywhere...

Java for Wireless Devices

Nowadays, mobile computing is becoming one of the vastest and most grown areas of technology, including mobile phones, pagers and personal digital assistants (PDAs) (Wilding-McBride, 2003). This environment is known to be very limited in terms of resources such as memory, processing power and display capabilities if compared to typical desktop computers. These limitations increased the need for more robust and carefully written software in order to suit the requirements of the target device.

Mobile Devices Constraints

Constrained Computational Capability

A typical desktop is powered using unlimited power supply, so it can run at high speed and dissipate large amount of heat, which is not the case for mobile devices which rely on a limited source of power consisting of small batteries. Therefore, mobile devices' manufacturers usually choose relatively low-power and low-speed CPUs in order to conserve battery life and hence reduce the frequency of charging batteries. Reducing CPU frequency reduces its computational power, which affects the usability of applications making them slower. This problem can be reduced by performing as much processing as possible on another computer (e.g. remote server).

Constrained Memory Size

Most of mobile devices have limited

memory size which implies that developers must manage memory usage carefully, especially if a programming language like C or C++ is used. The Java language introduces very important feature that consist of an Automatic Garbage Collector which frees memory from unused objects and helps to optimise memory usage (Knudsen, 2003).

Constrained Peripherals Capabilities

Almost all wireless devices have small screen size which limits the number of components to be displayed. In addition, they have limited input capabilities like keypads especially mobile phones which constrain the user inputs to the application. Hence, developers should consider Human Computer Interaction issues associated with the usability of wireless applications especially the Graphical User Interface (GUI). An application can be considered as approachable if the number of components displayed is reasonable, so the user does not need to scroll down the screen.

Java

Java is a very powerful Object Oriented Programming (OOP) language. It has been used in many areas of software development including the development of mobile applications. There are many advantages of using Java for developing mobile applications over other languages such as C++ and C. The main advantage of Java over other languages is the portability feature. Mobile Java technologies (e.g. MIDP, CLDC etc...) are now well supported

in millions of mobile devices. This allows developers to write applications at once and deploy them to any device that supports Java. This frees developers from developing platform dependent application that can run only on a limited number of devices. One of the great benefits of Java is the Automatic Garbage Collector. The Garbage Collector is a Java tool that frees dynamically allocated memory that is no longer referenced (i.e. unused objects). It relieves programmers from the burden of freeing allocated memory. Java applications development time is shorter if compared to C and C++, and the code size is relatively smaller, and it also provides very rich Application Program Interface (APIs) mainly consisting of the Mobile Information Device Profile (MIDP) and Connected Limited Device Configuration (CLDC), which has become industrial standards. These are very powerful libraries and available in almost all mobile devices nowadays.

The main disadvantage of using Java is its restively slow execution and huge memory requirements. This is because Java source code is compiled to bytecode which then needs the Java Virtual Machine to interpret it. This means that Java is not compiled directly to native code in order to run directly on the hardware (that is what makes it platform independent). This makes Java programs slower than its counterparts written in C or C++ using native APIs. In addition, although the Automatic Garbage Collector is a big advantage for Java, it has drawbacks. When the Garbage Collector is running, it consumes CPU cycles and occupies quite significant amount of memory. Nevertheless, wireless Java technologies are designed to cope with such limitations.

Connected Limited Device Configuration

(CLDC) is a fundamental part which provides the most basic libraries and virtual-machine capabilities that must be included in any Java 2 Micro Edition (J2ME) implementation.

Mobile Information Device Profile (MIDP) includes a set of Java API for developing user interface, networking capabilities, end-to-end security, multimedia and gaming functionality. Both CLDC and MIDP specification is developed through the Java Community Process (JCP). MIDP provides developers with a platform for developing and securely deploying optimised, graphical and networked applications.

The combination of MIDP and CLDC provides the core application platform required by mobile applications, consisting of standardised Java runtime environment and a rich set of APIs. Using MIDP, developers can build applications once and then deploy them to a vast range of mobile devices. MIDP has been widely adopted as the platform of choice for mobile applications. Hence, it is deployed globally on millions of mobile phones and PDAs taking advantage of the features of MIDP and especially portability.

Development Environments

There are several mobile application development environments that provide implementations of the Java standards MIDP and CLDC. These environments can be used to build, test and deploy Java application to any Java enabled wireless device. These environments are freely available for non-commercial purpose from their official websites.

The Java 2 Platform, Micro Edition (J2ME) provides a robust, flexible environment for applications running on consumer devices, such as mobile phones and PDAs,

as well as a broad range of embedded devices. Like its counterparts for the enterprise (J2EE), desktop (J2SE) and smart card (Java Card) environments, J2ME includes Java virtual machines and a set of standard Java APIs defined through the Java Community Process, by expert groups whose members include leading device manufacturers, software vendors, and service providers [3].

J2ME provides developers with useful tools for building, testing and debugging mobile applications. The first and the main tool is the emulator which emulates an MIDP device on a desktop. It also includes a memory monitor that shows the total memory used by the application and a detailed memory usage per object. A profiling tool is included to calculate how much time was spent in each method call and how many times each method was called (method call information).

IBM WebSphere Device Developer provides an integrated development environment based on Eclipse technology for building, testing, and deploying Java™ 2 Micro Edition (J2ME™) applications. The major component of this tool is the IBM Everyplace Micro Environment which represents the implementation of the MIDP and CLDC standards [4]. One of the main features of Studio Device Developer is that it can be used in conjunction with various devices' emulators and simulators such as Palm OS and PocketPC (figure 1 shows a screenshot of this software).

SuperWaba is an open-source software development platform for PDAs (Personal Digital Assistants) and Smartphones. The SuperWaba Software Development Kit (SWSDK) consists mainly of SuperWaba Virtual Machine (SWVM) which uses the "write once run anywhere" concept which provides portability to developed applications with rich set of user inter-

face controls and functionalities [5]. Any Java IDE can be used to develop SuperWaba based applications. It allows easy debugging through an applet that emulates the target devices on the desktop.

Conclusion

J2ME delivers the power and benefits of Java technology to consumer and embedded devices. It includes flexible user interfaces, a robust security model, a broad range of built-in network protocols, and extensive support for networked and offline applications that can be downloaded dynamically. Applications based on J2ME specifications are written once for a wide range of devices, yet exploit each device's native capabilities. The J2ME platform is deployed on millions of devices, supported by leading tool vendors, and used by companies worldwide. In short, it is the platform of choice for today's consumer and embedded devices. ■

Additional Resources

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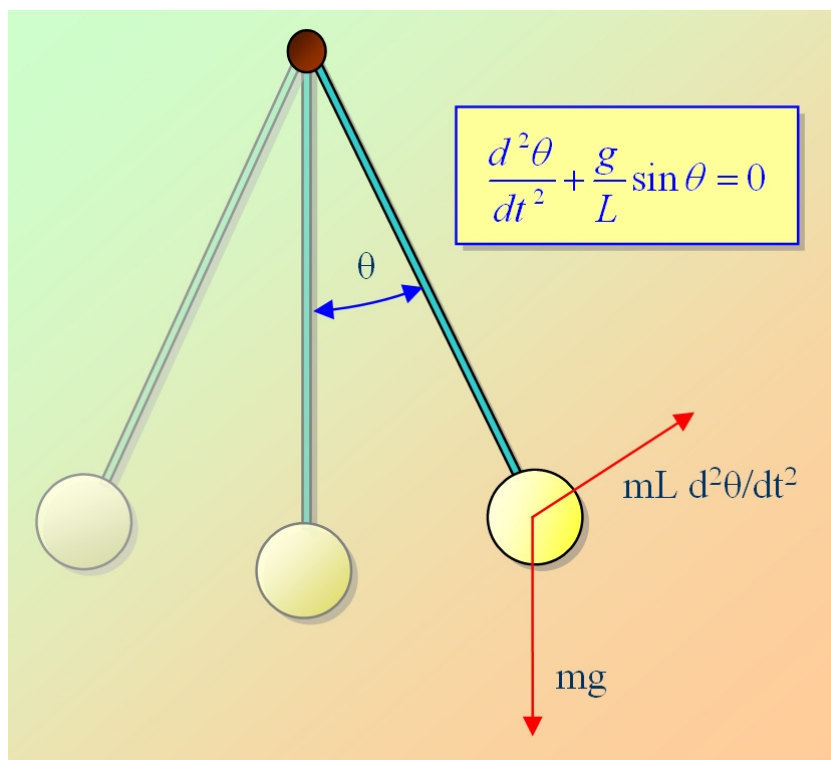
THE Pendulum

How can we solve the Nonlinearity Problem?

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Predicting the behaviour of many natural systems can be very difficult, if ever possible! The weather, for instance, is one of these rather complicated systems that scientists remain unable to accurately predict. The Lorenz equation, which models the weather in a simple manner, proves that such a system is chaotic, where it is impossible to accurately predict its future behaviour. Without diving into the world of chaos, the main reason for these systems to be so hard to analyse is due to the fact that they are 'Nonlinear'. In other words, they cannot be broken into smaller parts, solved separately, and then recombined to form the answer (the superposition principle fails). However, if these systems are unsolvable because of their nonlinearity, can we still understand their behaviours?

In this study, we will try to demonstrate how the dynamics of relatively "simple" nonlinear systems are extremely "complex" in nature and show how graphical methods can help to describe their behaviour.



Above
Figure 1: Simple ideal pendulum.

First of all, what is a 'dynamical system'?

"The notion of a dynamical system is the mathematical formulation of the general concept of a deterministic process. The future state of many physical, chemical, biological, economical and even social systems can be predicted to a certain extent by knowing their present state and the laws governing their evolution. Provided these laws do not change in time, the behaviour of such a system could be considered as completely defined by its initial state. Thus, the notion of a dynamical system includes a set of its possible states and a law of the evolution of the state in time." (Kuznetsov 1995)

Dynamical systems evolve with time by changing their states, and they can be divided to two major groups; continuous-time and discrete/integer-time dynamical systems, while the former could be described by differential equations, the latter would be described by iterated maps.

The pendulum is probably one of the first dynamical systems you studied in school (Fig.1). It is very likely that you were introduced to an ideal mathematical pendulum; a simple harmonic oscillator, where numerous simplifying assumptions were taken into account. This ideal pendulum would be free of air resistance and have no friction at the pivot; it would also have a weightless rigid rod instead of the string, therefore, it will only swing in a vertical plane rather than three-dimensional space. In order to further simplify this system, gravity is usually assumed to be constant and act vertically downward.

Although it may seem irrational to study an imagi-

nary ideal pendulum that cannot even exist in a laboratory setting, science has often made progress by studying simple abstractions when more realistic models were too complicated and confusing. (Stewart 1997).

The state of the pendulum is sufficiently described if the angle at which it hangs at any given time is known. By applying the Newton's law of motion on the pendulum system, a differential equation would be obtained involving the second derivative of that angle, together with some other variables such as the length of the string and the gravity acceleration constant, and hence, the subsequent step would be to solve the equation. Surprisingly, this is desperately hard, involving complicated items called elliptic functions. Therefore, the only way to solve the pendulum equation would be to cheat a little bit!

You may wonder why the equation is so hard to solve. In fact, the force acting on the pendulum is almost, but not quite, proportional to the angle between it and the vertical (the sine component presents a nonlinear element in the equation). Since mathematics is an exact science, 'Not quite proportional' does not essentially mean 'proportional', no matter how small the discrepancy is. Nevertheless, as we seem to have no other alternative, the standard of rigour will be lowered for the sake of progress by completely ignoring the small discrepancy and analysing equations for a fake pendulum free of the nonlinear sine component. The solution to this fake system, which is available in literature, is now very simple. If starting at time zero, the pendulum is pulled sideways to form an angle (θ^*) with the vertical then released, the angle θ at time t would be:

$$\theta = \theta^* \cos(\sqrt{\frac{g}{L}} t)$$

where g is the acceleration due to gravity and L is the length of pendulum.

In a similar fashion to the cosine curve, the angle of the pendulum wiggles between θ^* and $-\theta^*$, where angles to the left of the vertical are considered negative and those at the right, positive. The pendulum swings from left to right, between angles θ^* and $-\theta^*$, in a periodical manner that repeats the same motion over and over again. Therefore, the time taken to repeat this motion cycle is:

$$2\pi\sqrt{\frac{g}{L}}$$

where this period is constant for a given pendulum at any initial conditions.

The Phase Portrait of the Pendulum

Monitoring the position θ and velocity v of a pendulum in time is a prerequisite to assessing its behaviour. If the pendulum is set going at time zero with θ being plotted horizontally and v vertically at every hundredth of a second, a curve in the (θ, v) plane will be obtained, forming a trajectory corresponding to the chosen initial position and speed (Figure 3).

Varying the initial conditions would result in different trajectories, which form a family of curves that would cover the entire plane. For the 'fake' pendulum, these curves are concentric circles, whereas, the picture has more structure for a 'genuine' pendulum; looking like an eye with eyebrows and wrinkles brought on by too much oscillation (Figure 4).

How is this done?

The Law of Conservation of Energy, which is a mathematical consequence of Newton's laws of motion, states that the total energy, kinetic plus potential, remains the same throughout the motion (note here that friction is assumed absent!!). By choosing the mass and length equal 1, the kinetic energy of the pendulum is $\frac{1}{2}v^2$, and the potential energy can be taken to be $-g \cos \theta$. Therefore, it can be deduced from the Law of Conservation of Energy that along any trajectory

$$\frac{1}{2}v^2 - g \cos \theta = \text{constant}$$

Solving for the velocity v , we have

$$v = \pm\sqrt{\text{constant} + 2g \cos \theta}$$

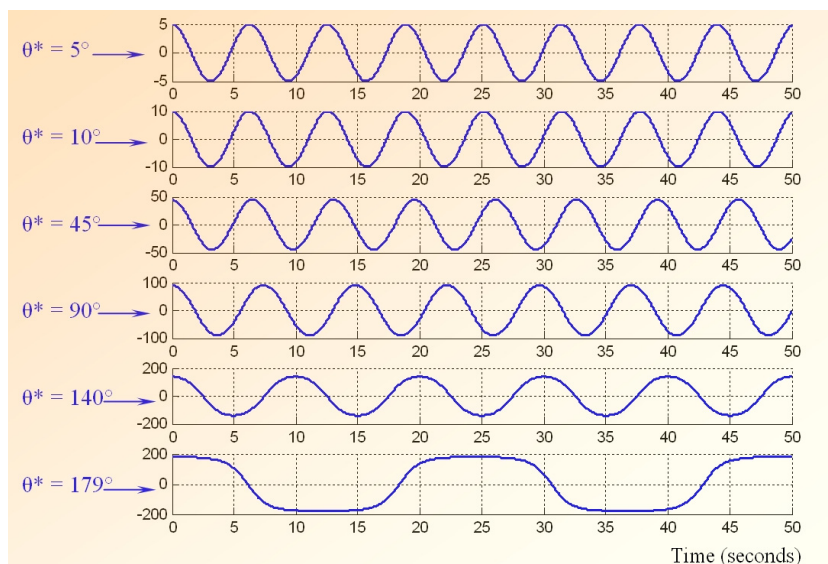
Using this formula, v can be plotted as a function of θ for any given constant value. If the term under the square root sign becomes negative, it can be ignored, otherwise two points can be plotted on the vertical line through θ ; one at

$$v = -\sqrt{\text{constant} + 2g \cos \theta}$$

, and one at

$$v = +\sqrt{\text{constant} + 2g \cos \theta}$$

An oval-shaped curve is obtained in this particular case, where there are no points at all if the constant is smaller than $-2g$ and only one single point is



Above
Figure 2: Oscillation of the nonlinear pendulum (Matlab simulation). The waveform is sinusoidal only when θ^* is small (equal to or smaller than 10).

obtained if it is $-2g$. The corners at the end of the oval become sharp if the constant equals $+2g$, and when greater than that, it would give rise to two separate curves.

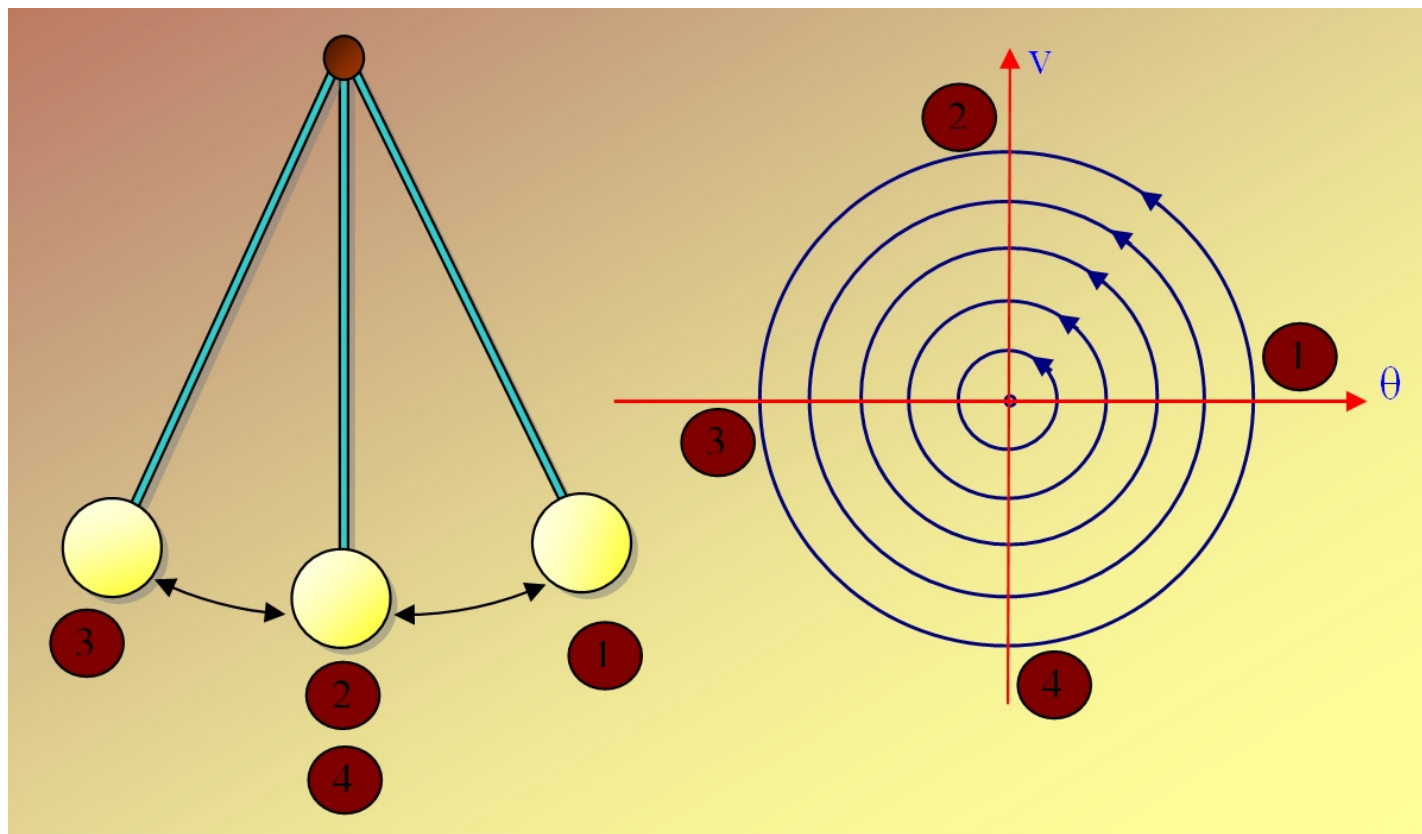
When the whole system is put together, the different trajectories of the pendulum form a picture that highly resembles the 'eye' (Figure 4); the single point is the pupil, the ovals are the iris, the oval with sharp corners is the edge of the eye, and the separate lines are the eyebrows (above) and the wrinkles (below). In addition to this simplified interpretation, Figure 4 can also be explained in terms of the dynamics of the pendulum, for instance, the position where the pendulum just hangs vertically and doesn't move, with both θ and v being constant is the single isolated point.

The standard oscillations of the pendulum are represented by the closed ovals. If you imagine the pendulum at the bottom of an oval (position θ equals zero), it would be hanging vertically downwards and halfway through a swing, with negative velocity if it is swinging to the left. Moving further round the oval θ becomes negative as v equals zero at the furthest point of the swing, where the pendulum turns back to go to the other way.

As the pendulum moves to the right, v becomes positive until it reaches its maximum at θ equals zero. At the furthest distance to the right, v plummets to zero and the pendulum returns to its original position, where the cycle would be repeated over and over again.

The eyebrows represent the propeller-like trajectory states where v is always positive, while θ varies from -180° to $+180^\circ$, giving rise to an infinite rotatory motion in the same direction. The lower wrinkle in the 'eye' represent analogous motions but clockwise instead of anticlockwise.

Moving on to the oval with corners; this trajectory represents the state where the pendulum changes from side-to-side swings and becomes a propeller. If the pendulum were held vertically then released, it would follow this path, the edge of the eye. In fact, that's not precisely correct; the pendulum would remain balanced at a single point (the corner of the eye), while the whole state is extremely unstable.



Therefore, the slightest disturbance will cause the pendulum to fall.

Above
Figure 3: Phase Portrait of a fake pendulum.

Below
Figure 4: Phase portrait of a genuine nonlinear pendulum.

Does This Mean We Solved the Pendulum Equation?

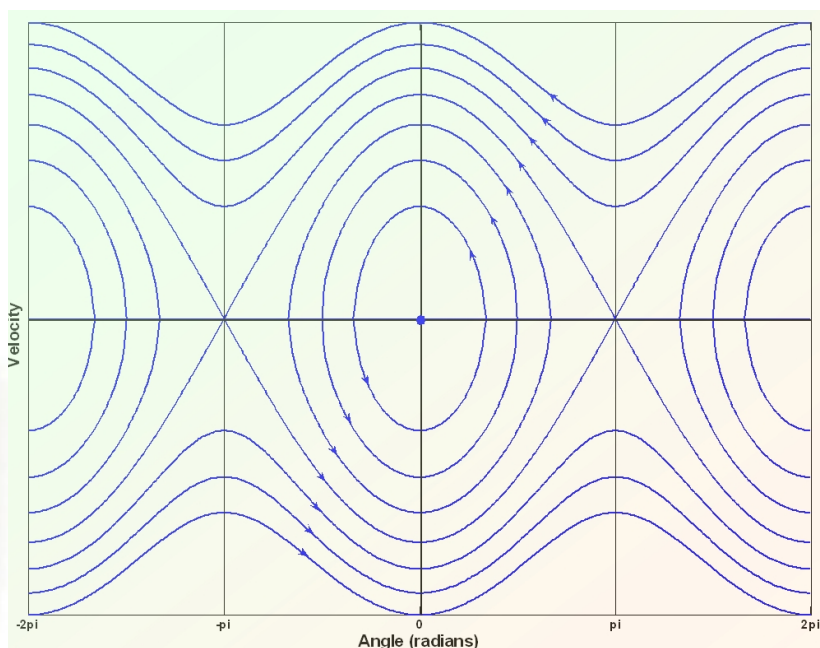
Although the curves were plotted using a formula, the pendulum equation remains unsolved, and to do so both θ and v should be specified for each time t , yet t never appears! We tried to simplify the analysis of the pendulum behaviour to understand its nonlinear dynamics, and the sacrifice was the precise time-dependence. It is easy to notice that the phase portrait of the pendulum provides no insight in the periods' length. On the other hand, it gives a consistent and persuasive picture of all possible motions of a genuine, though idealised, pendulum.

Finally, despite the aforementioned analysis, a real physical pendulum with friction at the pivot, air resistance and a real string would require a longer and more rigorous analysis. Besides, if this is the case for a simple pendulum, what about forced, double and even worse, chaotic pendulums? What about a bridge, space shuttle or a human heart? The simple answer is that we can never predict the exact behaviour of many systems, but only use mathematical methods with the aid of appropriate simplifications to understand their qualitative rather than quantitative behaviour.

Great thanks go to Stewart, I., whose review on The New Mathematics of Chaos has greatly inspired this study. ■

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CLINICAL TRIALS in drug development: An Introduction

Clinical trials form an integral part of the drug development process, as they investigate the safety and efficacy of potential new drugs. Clinical trials have evolved remarkably over the past few decades mainly to improve the testing procedures and data interpretation, which would consequently increase the reliability of clinical trials as a tool of testing new chemical entities. However, the recurrence of discovering 'new' side effects of drugs, which are already on the market, raises the question of how reliable clinical trials are.

Due to the significance of clinical trials in the drug development process and the lack of knowledge regarding this subject among science students and some scientists, we decided to run a three articles series examining clinical trials. The first two articles are aimed to achieve two points; firstly, provide an introduction to clinical trials, i.e. history, types and importance, and secondly, examine the procedures involved in assessing Pharmacokinetics and Pharmacogenetics properties during clinical trials. The third article will include examples of when testing during clinical trials went wrong and will comment on the future of clinical trials.

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Clinical trials are a method for comparing objectively, by a prospective study, the results of two or more therapeutic procedures (Rang et al, 1999). These results are obtained by testing the potential treatments on human subjects. However, for a drug to get to this stage, i.e. be tested on humans, it has to be tested on animals first in a stage known as preclinical trials. At this stage, the new chemical entities with therapeutic potential are tested, mainly, for their efficacy and toxicity. Nevertheless, the pharmacokinetics properties of the drug molecule(s) could also be examined at this stage. Preclinical trials are carried out by microbiologists on bacteria and biologists on animals (Thomas, 2000), and they are conducted in living organisms (in vivo) and in artificial environments (in vitro). Successfully passing preclinical trials is one of requirements needed for the drug to undergo clinical trials. The other requirement is obtaining an approval (or a license) from the appropriate legal and ethical committee for conducting clinical trials (Thomas, 2000). This is due to the legal and ethical issues that can rise from conducting such trials. The ethical issues regarding clinical trials are outside the scope of this article.

Prior to carrying out a clinical trial, an agreed protocol which serves as a plan or guide must be established. The protocol covers the design of the trial, the Prior to carrying out clinical trials, an agreed protocol which serves as a guide or plan for conducting the trial, must be established. The protocol covers the design of the clinical trial, the medications and medical tests that should be used as well as who should and who should not participate in the clinical trial. The protocols of clinical trials must also be carefully designed to safeguard the participants and not to expose them to excessive and ethical risks. Protocols vary from one clinical trial to another depending on the drug being tested and the disease or condition for which the drug is being developed.

Why Are Clinical Trials Important?

The drug discovery process yields a huge number of compounds, which are initially designed for the treatment of a particular disease or condition. In fact, the number of compounds generated at the drug discovery phase has increased dramatically over the past few years due to

the development in solid phase synthesis and computer based drug design. However, only very few of those compounds make it into the market. This is due to the absence of/or poor pharmacological activity, poor pharmacokinetic profiles and/or safety issues. These compounds' characteristics are revealed during the pre-clinical testing and/or during clinical trials. The data obtained from clinical trials help understand the effects of the drug on the body (Pharmacodynamics) and the way the drug affects the body in time (Pharmacokinetics) (Neal, 1997). Moreover, the data gives an indication of the pharmacological activity of the drug. All of these findings are then used to make a decision on the drug molecule. The decision could vary from structure modification, dropping off the compound from drug development process or licensing and marketing the drug. This shows the importance of clinical trials in the drug development process.

What Do We Know About the History of Clinical Trials?

The first clear evidence of clinical trials

being conducted appeared in 1948 in a publication by the UK Medical Research Council (Machin et al, 2004 and Medical Research Council, 1948). This trial investigated streptomycin as a potential treatment of pulmonary tuberculosis. However, earlier examples of trials conducted to investigate therapeutic efficacy of herbs do exist. The earliest example of clinical trials appeared in the Book of Daniel, which was written around 150BC (Machin et al, 2004). The trial was of a nutritional experiment using a control group, as given below.

"Then Daniel said to the guard whom the master of the eunuchs had put in charge of Hananiah, Mishael, Azariah and himself, 'Submit to us this test for ten days. Give us only vegetables to eat and water to drink; then compare our looks with those young men who have lived on the food assigned by the king, and be guided in your treatment of us by what you see.' The guard listened to what they said and tested them for ten days. At the end of ten days they looked healthier and were better nourished than all the young men who had lived on the food assigned them by the king. So the guard took away the assignment of food and the wine they were to drink, and gave them only vegetables." (Machin et al, 2004; Slotki et al, 1951).

Another record of clinical trials can be found in a 14th century letter from Petrarch to Boccaceto (Machin et al, 2004). It was a trial that compared the survival of two groups affected by the same disease, but one was on the doctor's drugs while the other group relied on nature's instinct. Interestingly, this trial took into account the age, habits and surroundings of subjects used in the trial. Clinical trials continued to be employed from the fourteenth century until the nineteenth century, and examples of these do exist. In the nineteenth century there was the first indication of using the numerical aspect to comparing treatments. The trial was carried by a Canadian pathologist named Pierre-Charles-Alexandre Louis. In this trial Louis compared the results of treatments on groups of patients with similar degrees of disease (Machin et al, 2003), as given below.

"I came now to therapies, and suppose that you have some doubt as the efficacy of a particular remedy: How are you to proceed?...You would take as many cases as possible, of as similar description as you could find, and would count how many recovered under one mode of treatment, and how many under another; in how short a time they did so, and if the cases were in all respects alike, except in the treatment, you would have some confidence in your conclusions; and if you were fortunate enough to have a sufficient number of facts from which to deduce any general law, it would lead to your employment in practice of the method which you had seen often set suc-



cessful" (Machin et al, 2004).

Since then clinical trials have been evolving for better and new procedures of testing and statistical analysis have been adopted. This development led to the introduction of many new components to clinical trials including randomization and blinding. Clinical trials, nowadays, have become very complicated processes which require precise design, implementation and data interpretation. Thus, they are dependent on a team which is made of scientists from different disciplines; chemists, pharmacists, doctors, statisticians...etc. This involvement of scientists from different disciplines is aimed to achieve better design and conduction of clinical trials. In addition, it allows better interpretation of the data obtained.

What Are the Types of Clinical Trials?

The purpose of conducting clinical trials pretty much determines the type of the trial. Generally, there are four types of clinical trials: treatment, prevention, diagnostic (also known as screening) and quality of life trials.

Treatment trials study the efficacy and safety of new drugs, combination of drugs, new approaches to surgery or therapy, or new methods. Examples of treatment trials include those carried out for testing new chemotherapeutic agents for the treatment of a certain type of cancer.

Prevention trials could be carried out to achieve two points. Firstly, seek new ways of preventing the recurrence of the disease in people who suffered from it before and, secondly, find new ways of preventing the disease in the first instance. The testing in prevention trials does not only involve using drugs, but vitamins, minerals, vaccines and lifestyle changes could also be employed.

Diagnostic trials, as the name suggests, are studies conducted to explore better procedures for diagnosing a particular disease or condition. In some cases, trials are carried out to find out the best test or

procedure of detecting certain diseases or health condition. These types of trials are known as screening trials. Quality of life trials, also known as supportive care trials, are investigations aiming at finding ways of improving the quality of life of patients with chronic illnesses, e.g. evaluating the coronary obstructive pulmonary disease (COPD) causing habits such as smoking.

What Are the Different Phases of Clinical Trials?

The types of human clinical trials employed during the development of new drug treatments are generally divided into four different phases. The first three phases occur prior to a license being granted, while the fourth is after. Each phase varies in size, character and focus (ABPI). The explanation of clinical trials phases summarized below is for the drug development clinical programs not the other types of trials.

Phases I trials

Phase I clinical trials are the first investigations conducted in humans and they may involve healthy individuals and/or volunteers who do not suffer from the disease or condition under investigation (Harman, 2003). Numerous phase I clinical trials are conducted using less than 20 volunteers, but the number in most cases is within the range of 50-100 (Harman, 2003). The aim of this phase is to determine the metabolism of the new drug as well as its pharmacokinetics and pharmacodynamics profiles. This would help understand the behaviour of the drug inside the body. More importantly, it would help determine what doses should be used and at what frequency.

Phase II trials

Unlike phase I clinical trials, phase II clinical trials are conducted in a small number of patients rather than healthy volunteers. The number of patients used at this stage is usually within the range of 100-300, and they all suffer from the disease or condition for which the drug has been developed (ABPI). Phase II trials often yield a wide variety of information regarding the new drug being tested. They are the first to determine the existence of potential therapeutic effects in patients (Machin et al, 2004). Moreover, they provide a thorough investigation of the safety of the drug, i.e. any possible side effects. In general, phase II trials set the scene for subsequent confirmatory phase III trials (Machin et al, 2004).



Phase III trials

Phase III trials are the major and most expensive stage of the clinical development process. They involve a larger number of volunteers than in phase II (1000-5000 patients)(ABPI and Harman, 2003). These patients should be selected so they come from different regions of the country or even from different countries (Harman, 2003). Using a large number of patients at this stage enables statistical interpretation of the results. Unlike phases I and II, three different 'drugs' could be used in phase III; the drug being developed, a placebo and a known market leader (Harman, 2003). In most cases, the trial is carried out 'double-blind' meaning that the subscribers do not know which patients are taking the potential drug and which ones are on the placebo or the market leader. The groups are then switched during the trial in order to ensure objective and statistical assessment of the treatment under investigation (Harman, 2003). The data derived from phase III studies will give an assessment of the drug's safety and efficacy.

Phase IV trials

Phase IV trials are sometimes called post-marketing surveillance. They are conducted for drugs that have already been granted a marketing authorization. The objective behind these studies is mainly to answer marketing questions, while it is very rare for these studies to be conducted on the purpose of answering research questions. In fact, one of the common reasons for undertaking phase IV trials is to investigate the possibility of expanding the indications listed on a marketing authorization (Machin et al, 2004). Such studies could also yield more safety data. Although phase IV studies are mostly carried out by pharmaceutical companies, some academic departments could carry out these studies and they should also be

Summary

Phase I

It is conducted in small group of healthy human subjects. The objective is to investigate the new drug's pharmacodynamics, pharmacokinetics and toxicity.

Phase II

Unlike phase I, phase II is carried out in patients to investigate the dosing regimen and safety.

Phase III

Evaluates the efficacy of the drug, and the data obtained forms the main core of the data submitted for the new drug's registration.

Phase IV

These investigations are done after the product's registration. They are mainly for marketing purposes.

considered as phase IV trials rather than an academic research project.

Conclusion

In summary, Clinical trials have evolved considerably since they were first employed. They have moved from being an efficacy investigation to a practice revealing numerous properties of the new chemical entities. These properties are characterized using different approaches, mainly by evaluating the pharmacokinetics and pharmacogenetics of these new products. Nowadays, these properties are tested over four phases, each with a different objective. Eventually, the data obtained is used in deciding the fate of the compound being tested. The decision varies from structurally modifying the drug to improving some of its properties or in the worst scenario dropping the drug from the development process. On the other hand, if the clinical data is positive, it is then used to justify the effective and safe use of the new chemical entity in treating certain diseases and conditions.

The procedures employed in evaluating the pharmacokinetics and pharmacogenetics of new chemical entities during clinical trials will be discussed in the second article of the Clinical Trials series, which will be published in the next issue of IBScientific. ■

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The field of polymers and scaffolds for tissue engineering has reached an advanced phase and is maturing rapidly. This technology has been applied to engineering of bone, cartilage, liver, and bladder tissues, and is a promising new solution to organ failure. However, today, tissue engineering is rapidly evolving from the initial proof-of-principle demonstrations of feasibility to the development of products intended for widespread clinical use.

Since the outermost surface of a scaffold is immediately located at the interface with cells or tissues, the surface properties will guide cell-material interactions and, in return, affect cell adhesion (Dobkowski et al., 1999). Thus, it is also important that the scaffold surface is conducive to cell attachment and subsequent tissue growth. It is then desirable to be able to adjust surface properties to suit the intended application, often without altering other properties of the scaffold, like its mechanical strength or thermal properties. In fact, a number of critical engineering design issues must be addressed during this

transition to enable large-scale manufacture and use of a variety of engineered tissues. These challenges include techniques for modification of scaffold surfaces that carry out very sophisticated signalling needs and enhance cellular adhesion. Such modifications usually involve coating surfaces with extracellular matrix (ECM) proteins, which provides an adhesive interface between the scaffold material and the cells to resemble the native cellular milieu.

Therefore, the present review aims to investigate the benefits of surface engineering and scaffold modification for tissue engineering applications. First, the important role of synthetic biodegradable polymeric scaffolds that constitute the support for cells to proliferate into a functioning tissue will be addressed, highlighting the limitations of these materials and the need to find other ways to create scaffolds with complex internal features. Subsequently, a description of the surface physical interpenetrating network (SPIN) technique exploited in surface engineering and scaffold improvement will be discussed and finally, a successful application for tissue engineering "Bone regeneration"; in relation to scaffold modification, will be reviewed.

Tissue Engineering: Overview

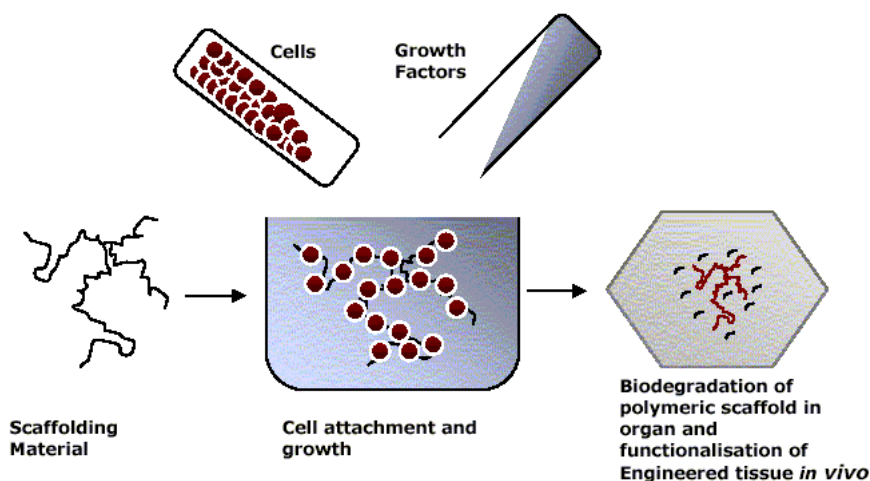
Tissue engineering (TE) is an exciting new area of interdisciplinary research and development that has the potential to revolutionise methods of healthcare treatment and has shown great promise in generating living alternatives for harvested tissues and organs for transplantation and reconstructive surgery. It applies the principles and methods of engineering and life sciences towards the fundamental understanding of structure-function relationships, in normal and pathological mammalian tissues, and the development of biological substitutes to restore, maintain, or improve tissue function (Langer et al., 1993).

The field of tissue engineering will open up new areas of regenerative medicine allowing a wide range of tissue reconstruction and repair possibilities for chronic conditions. The development of devices for implementation into damaged tissue namely polymer scaffolds, will assist tissue repair, either by aiding tissue adhesion, orienting cells correctly or trapping inflammatory cells (Shalak et al., 1988). Indeed, cells are generally implanted or seeded into an artificial structure capable of supporting three-dimensional tissue formation. Such devices, usually referred to as 'scaffolds'. These allow cells to attach and grow in a three dimensional space while nutrient flow is maintained throughout the matrix (Figure 1).

TISSUE engineering

How Will Surface Engineering Prosper its Applications?

Faiza MEFTAH
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Above

Figure 1: Schematic diagram showing the concept of tissue engineering

Scaffolding materials (temporary synthetic extracellular matrices) are designed as a three-dimensional mirror image, on which cells grow and regenerate the needed tissues. Because the scaffolding materials are biodegradable, they will resorb after fulfilling the template function.

To achieve the goal of tissue reconstruction, the scaffold must have a large enough surface area to allow sufficient room for cell attachment which is required for tissue growth. Besides, the formation of pores in the polymer increases sites for cell attachment, and the pore size and porosity can be controlled to give the structure varying physical characteristics such as strength and elasticity. The pores are interconnected to allow for essential nutrient and gas exchange for all cells in the scaffold. These characteristics are required for tissue growth and differentiation into a functioning organ.

Scaffolds may be constructed from many different materials (natural and synthetic, biodegradable and permanent). However, this review will solely focus on the synthetic polymers.

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Synthetic Polymers as Packaging Materials for Tissue Engineering

Degradable polymeric biomaterials have been widely used to construct temporary scaffolds for tissue engineering and drug delivery applications. Major interest has been centred in the biodegradable syn-

Polymer	Polymer repeat unit structure
Poly(glycolic acid)	$\left[\text{O}-\text{CH}_2-\text{C}(=\text{O}) \right]_n$
Poly(lactic acid)	$\left[\text{O}-\underset{\text{CH}_3}{\text{CH}}-\text{C}(=\text{O}) \right]_n$
Poly(glycolic-co-lactic acid)	$\left[\text{O}-\text{CH}_2-\text{C}(=\text{O})-\text{O}-\underset{\text{CH}_3}{\text{CH}}-\text{C}(=\text{O}) \right]_n$

thetic polymers namely poly (glycolic acid) (PGA), poly (lactic acid) (PLA), and their copolymers poly (lactic-co-glycolic acid) (PLGA) (Holland et al., 1992) (table 1). This particular family of degradable esters is attractive for tissue engineering since they are readily available and can be easily processed into a variety of structures and more predictable lot-to-lot uniformity than can materials from natural sources. In addition, they act as remodelable provisional matrix into which cells from the neighbouring tissue can be induced to migrate (Mooney et al., 1996), their biodegradation can be tailored by varying the concentration of each monomer (PGA and PLA), and they have already been approved by the Food and Drug Administration (FDA) for use in a number of human clinical applications (Chaignaud et al., 1997). However, their degradation is manipulated by other factors; some of which are crystallinity, molecular weight, copolymer ratio, porosity and site of implantation, and configurational structure (Guoping et al., 2000).

One of the current challenges in culturing a tissue is to select a polymer scaffold that meets the mechanical properties and degradation times required. The ideal polymer for a particular application should be configured so that it possesses the properties highlighted in table 2.

In general, an unstable backbone of the material leads to biodegradation. The most common functional chemical groups with hydrolytically unstable linkages are esters, anhydrides, orthoesters and amides. Factors that accelerate polymer degradation include an increased hydrophilic backbone, increased number of reactive hydrolytic groups in the back-

Left

Table 1: Biodegradable Polyesters.

Below

Table 2: Properties of the ideal polymer to be used in tissue engineering.

1. Appropriate mechanical strength to mimic *in vivo* conditions.
2. Rate of matrix regeneration close to biodegradability rate of the biodegradable polymer scaffold.
3. Does not invoke an inflammatory or toxic response.
4. Is metabolised in the body after fulfilling its purpose, leaving no trace (bio-absorbable)
5. Is easily processable into the final product form, either porous or compatible with a range of extremely hydrophilic additives (starch, salt) to create porosity
6. Demonstrates acceptable shelf life and is easily sterilised.

bone, less crystallinity, increased porosity and a larger surface area. Balancing each of these factors will allow an implant to slowly degrade and transfer stress at an appropriate rate to surrounding tissues as they heal. This is one of the major challenges facing TE research today.

Limitations of Current Tissue Engineering Scaffolds

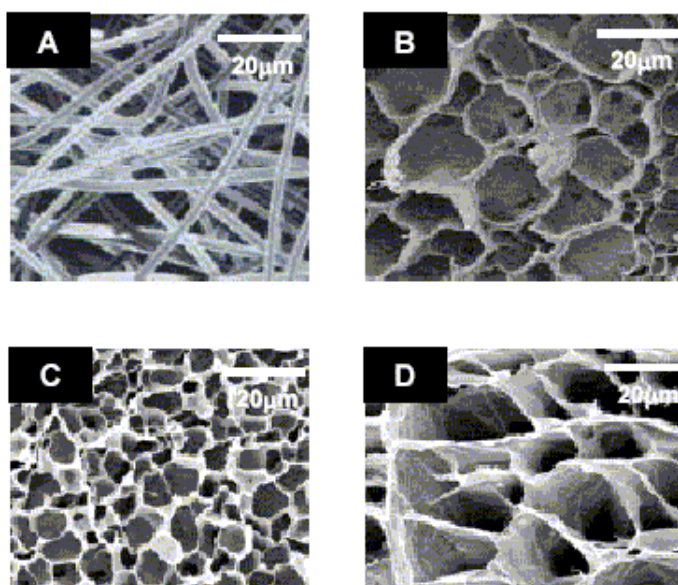
So far, the majority of polymers that are in use today for biomedical applications are based on polylactides and polyglycolides (Holland et al., 1992). While these have the necessary degradation and physical properties for use as sutures and drug delivery vehicles, they invoke a slight inflammatory response by the immune system making host acceptance an issue.

Tissue engineering causes several other problems. Mainly, cells in tissues and organs are arranged in distinct patterns that are dictated by cues given to proliferating cells during organ development (Curtis et al., 2001). These cues can be chemical, as in the presence of adhesion proteins or gradients of growth factors. At the same time, it is very well documented that topographical cues by the extracellular matrix may have significant effects upon cellular behaviour (Wilkinson et al., 2002). Indeed, the construction of fully biomimetic matrices containing all of the required chemical and topographical factors is not yet achieved. In this respect, scientists are focusing on the design of new implantable materials in which both topographical features and chemical cues act synergistically for cell attachment and proliferation (Langer., 1998).

A key attribute of any successful scaffold is its ability to support life and the normal physiology of cells. Immediately, any potential toxic effects of the scaffold must be addressed. Obviously, materials that are toxic are eliminated from consideration as scaffold components. However, there are also scaffold manufacturing considerations. Chemicals that are used to synthesise a scaffold may persist at low levels in the completed structure, presenting potential hazards to seeded cells or to the host (patient). Moreover, scaffolds must be capable of permitting normal developmental and physiological behaviour of cells.

Another limiting factor worth pointing out is the fact that these polyesters tend to be relatively stiff materials. While this may be an advantage in load-bearing applications, it becomes a disadvantage

Physical	Chemical	Radiation
Surface Physical Interpenetrating Network	Surface Hydrolysis	Plasma glow discharge
Langmuir-Blodgett film	Flame treatment	Ion beam treatment
	Surface grafting	Plasma polymerization



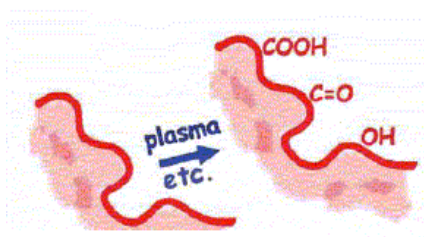
Top
Table 3: Methods of Surface Engineering.

Above
Figure 2: Examples of polymeric scaffolds used in tissue engineering.

A: a typical nonwoven scaffold; B: a 3-D porous biodegradable hydrogel network structure reinforced by a non-woven fabric; C, D: Hydrogels made up of poly (N-isopropylacrylamide) with large 3-D pore network structure.

Below
Figure 3: Schematic representation of surface modification via plasma-induced polymerisation. Creation of functional groups such as carboxylic acids, ketones, and hydroxyl functions at the polymer surfaces.

when mechanical compliance with soft tissue or blood vessels is required. Finally, none of these polymers provides a chemically reactive pendent chain for the easy attachment of drugs, crosslinkers, or biologically active moieties (James et al., 1996). Although simple poly(α -hydroxy esters) have performed well in



establishing the foundation and feasibility of tissue engineering, they may not be optimally suited for the construction of polymeric cell scaffolds serving a variety of applications.

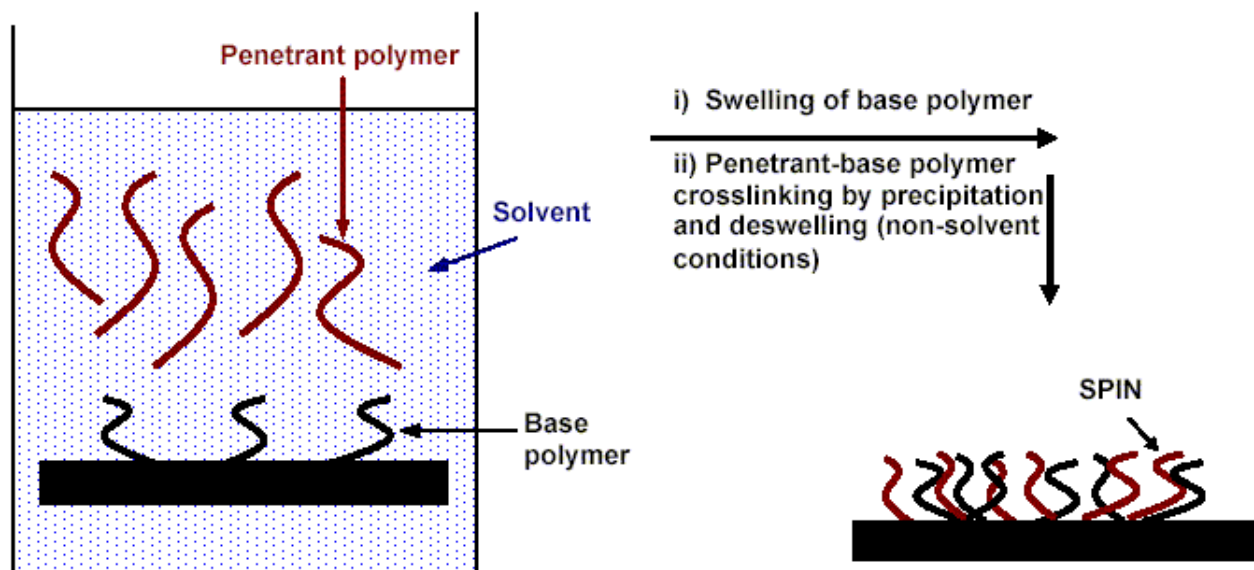
Surface Engineering & Scaffold Modification

Surface engineering offers a technology to alter interfacial properties without affecting the bulk characteristics of a material. Several methodologies have been considered and developed for altering the interactions of biomaterials with their biological environments by various means of physical, chemical, or radiation processes (Table 3).

Nevertheless, only two methods of scaffold surface modification: Plasma-induced polymerisation and surface physical interpenetrating network (SPIN); will be covered as they have gained a huge interest within the research community for their breakthrough outcomes.

Plasma-induced polymerisation

This is a clean technique which uses radio-frequency (RF) produced by low-



pressure glow-discharge and introducing gases such as Ar and O₂, to create active species (free radicals or peroxides) in order to initiate free radical graft polymerisation processes (Hsiue, 1993). This method is widely used for modifying the surface of materials to improve cell growth, protein binding and non-binding, and cell-specific attachment by controlling surface chemical structures, surface energies and/or surface charge states. Functional groups such as -NH₂, -OH and -COOH are most frequently grafted by means of plasma treatment of non-deposition gas such as NH₃, O₂, H₂O, etc (Yang, 2002).

It has been demonstrated that plasma polymerisation technique is a unique and powerful method for the improvement of surface characteristics such as chemistry, structure and wettability, without changing the biomaterial's desired bulk properties, i.e. strength and biodegradability (Ryou, 2003). However, the modified results will decline with time after plasma treatment, which will affect its further application.

Surface Physical Interpenetrating Network

This is a new technology for combining two or more polymers in a network form, at least one of which is polymerised and cross-linked in the immediate presence of the other(s) (Desai et al., 1992).

A common approach is to physically anchor a long-chain hydrophilic polymer in a supporting polymer network that is normally non-swellable in water. Conceivably, one end of the long hydrophilic polymer becomes entwined within the supporting polymer; hence the free end is able to become hydrated (Figure 3). Generally, the hydrophilic

Above
Figure 4: Modification strategy by Surface Physical Interpenetrating Network (SPIN).

polymer is dissolved in an organic solvent together with the polymer that will form the supporting matrix (Desai et al., 1992).

This modification strategy is performed by incorporating a complete coating of a polymer (penetrant polymer), of considerably different properties, into the surface of another polymer, swelling the surface of the polymer to be modified (base polymer) in a mutual solvent. Consequently, the penetrant polymer diffuses into the surface of the base polymer. This interface is stabilised by rapidly precipitating or deswelling the surface by placing the base polymer in a non-solvent bath (Desai et al., 1991). This resulted in entanglement of the penetrant polymer within the matrix of the base polymer at its surface in the structure called a surface physical interpenetrating network (SPIN) - (Figure 4).

Surface Engineering Applications

While several tissue engineering breakthroughs have been made, using different strategies of surface engineering, further progress in generating laboratory-grown tissues and organs remains a challenge for treating many diseases. Nonetheless, the application of information and principles obtained through years of research in several disciplines to the goals of tissue engineering has already resulted in several promising medical advances such as tissue engineered heart valve leaflets (Wilcox et al., 2003), bio-artificial skin (Pearson et al., 2002) and bone regenera-

tion (Yang et al., 2001).

The bone has a considerable potential for regeneration and therefore is a prototypic model for tissue engineering. This field is making new and important contributions to the treatment of the loss of skeletal tissue due to trauma or disease, based on the application of surface engineering principles, specifically, the surface physical interpenetrating network (SPIN) method. This is a promising approach for the development of an orthopaedic biodegradable material that allows osteogenic cells adhesion at a required site to promote considerable new bone formation (Figure 5).

Poly-lactic acid (PLA) and related poly(Hydroxyacids) are extensively exploited in clinical orthopaedics, and the ability to modify their surface through SPIN; by incorporating additional materials such as poly(ethylene glycol) (PEG) (Quirk et al., 2001), provides a new approach to promote adhesion and proliferation of osteoblasts selectively and significantly.

The incorporation of PEG into the biomaterial structure is physically created by entrapment of the modifying species at the PLA surface. Following exposure to a solvent/non-solvent mixture, PLA surface endures a reversible gelation enabling the PEG to diffuse into the swollen surface (Quirk et al., 2001). This results in generating non-adhesive material as well as immobilising several modifying groups, therefore producing a system that averts unwanted interactions nevertheless promotes osteogenic cells adhesion at desired positions such as around metal implants post-surgery, in fracture gaps, and within osteoporotic bone.

Vogt et al. (2005) at the Innovent

Institute in Germany have very recently designed new polymer-based scaffolds for bone tissue engineering. The scaffolds were based on novel difunctional oligolactone macromers that have been synthesised by ring-opening oligomerisation of various lactones (L-lactide, glycolide, p-dioxanone) in the presence of suitable diols and subsequent endcapping of the formed oligolactones with methacrylate moieties. The resulting scaffolds were found to be highly porous and their surface properties were optimised using SPIN. Preliminary in vitro studies on the cytocompatibility of the fabricated scaffolds and on osteoblast cultivation on the optimised polymeric materials demonstrated that the oligolactide based polymer networks possess an excellent biocompatibility and that they would represent promising candidates as scaffolds in bone tissue engineering in the future.

Conclusion

A large fraction of healthcare costs are attributable to tissue loss or organ failure. Conventional therapies, even if they have revolutionised medical practice, show several limitations; while transplantation is restricted by the donor shortage, mechanical devices cannot perform all of the functions of a single organ,

and therefore provide only temporary help.

With the progressive ageing of the population, age-related degeneration of organs is constantly increasing. Thus, the field of tissue engineering holds great potential for the development of synthetic polymeric scaffolds in support of tissues replacement for numerous tissue engineering applications. Ultimately, efforts to improve the surface of these scaffolds, ranging from chemical to radiation to physical strategies, will amplify therapeutic abilities in treating various diseases and vitalise the revolutionary approach of bioregenerative medicine and tissue engineering, yet, the future should prove to be even more innovative. ■

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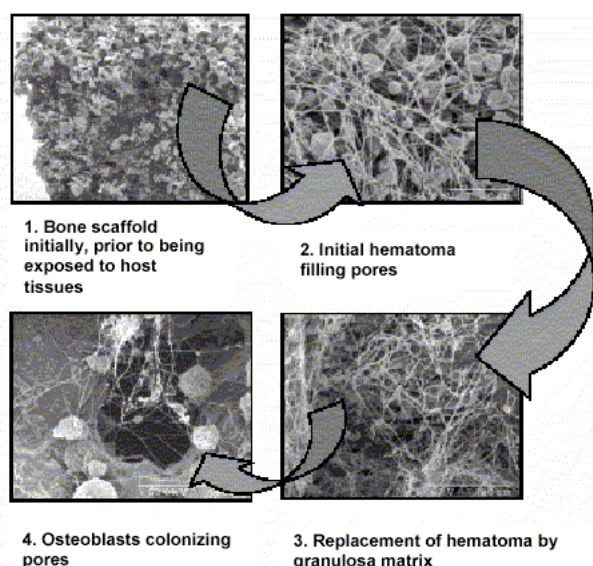
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Below

Figure 5: Sequence of cell/scaffold interactions following the hypothetical placement of a scaffold into a host bone environment. The surgical replacement of a scaffold into a host would result in hematoma formation filling the open-pore structure of the scaffold. As with any generalised healing sequence, the sequence of events in a bone host environment would follow the sequence outline below. In a longer time frame, the scaffold would be expected to degrade as osteoblasts make a new bone structure and fill both the pores and any voids created by degrading scaffolds.



Ibn Sina

The Prince of Medicine



<http://www.afghanland.com/history/ibnsina.html>

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Ibn Sina, 980–1037 C.E., was arguably the most famous physician, philosopher, mathematician and astronomer of his time. In the course of the 58 years of his life Ibn Sina wrote 99 books most of which in Arabic. These books became the language of religious, scientific and ordinary people in the entire Muslim world at that time. Ibn Sina's most recognisable work is the notoriously famous book *Al Qanun fi Al-Tibb*, which is known in the West as the "Canon". Ibn Sina was also famous for his quote "I prefer a short life with width to a narrow one with length", which was his usual reply to people requesting him to slow down and take life in moderation. Overall, Ibn Sina was certainly one of those philosophers and scientists who contributed hugely to science and who made the Islamic civilization such a colorful one.

Abu Ali al-Hussain Ibn Abdallah Ibn Sina, known in the West by the Latin name Avicenna, was born in 980 C.E. in the village of Afshana near Bukhara. In his childhood, Ibn Sina was very proficient in Arabic classics and the Quran and as he was growing up he devoted himself to Philosophy, Natural Sciences and Islam. At the age of 13, however, he turned his attention to Medicine which he found it to be "Not difficult". Nevertheless, Ibn Sina was generally troubled by metaphysical problems and in particular the works of Aristotle. However, these difficulties did not last for long as he, by chance, managed to obtain a manual from Al-farabi which solved his problems.

Although Ibn Sina was self-taught, he did receive some help from the best teachers of his time. Ibn Sina's expertise in Medicine was firstly tested at the age of 17 when he was asked to treat Nooh Ibn Mansoor, the King of Bukhara. The king, at that time, was suffering from an illness which even great physicians could not cure. Fortunately, the young Ibn Sina managed to treat the king and as a reward he was granted permission to use the King's uniquely stocked library.

The Death of Ibn Sina's father as well as the political instability at the Bukhara region changed the course of his life. Ibn Sina left Bukhara to Khorasan where he was acting as a physician during the day and, at evenings, running meetings with students discussing philosophical and

scientific issues. After leaving Khorasan Ibn Sina stayed in Guranj (Khwarazm) for a while where he served as a jurist. Then, he settled in Hamadan, west-central Iran, where he got involved in politics which at some stage forced him into hiding and later led him to prison. After his release



<http://www.ci.birmingham.mi.us/home/index.asp?page=864>

from prison, and following the death of the prince of Hamadan whom he was serving, Ibn Sina decided to leave Hamadan in 1022. He moved to Isfahan where he spent the rest of his life in peace. There, he acted as the advisor of the governor on scientific and literary matters. Worn out by hard work and hard living, Ibn Sina died at the age of 58, in 1037, and he was buried in Hamadan where his grave is still shown.

Ibn Sina wrote so many articles and books in a variety of fields including medicine, philosophy, psychology, geology, mathematics, astronomy and logic. However, he contributed most to medicine and philosophy as the majority of his publications are in those two streams. Ibn Sina's two most remarkable works are *Al-Qanun fi al-Tibb* (The Canon of Medicine) and *Kitab al-Shifa* (The Book of Healing).

Al-Qanun fi al-Tibb was divided into five chapters. Two chapters were on physiology, pathology and hygiene while another two were devoted to the methods of treatment. The last chapter included the preparation of some remedies and the author's observations. This book was firstly translated into Latin in 1187 A.C. and soon was established as the textbook for medical education throughout Europe. In the late fifteenth century

there were sixteen editions of *Al-Qanun fi al-Tibb*, fifteen of which were in Latin and one was in Hebrew. Later, the book was translated into English. The contribution of *Al-Qanun fi al-Tibb* to medicine was summarized by Dr. William Osler, author of the *Evolution of Modern Science*, as he wrote "The Qanun has remained a medical bible for a longer period than any other work."

Kitab al-Shifa is a philosophical encyclopedia dealing with a vast sum of knowledge ranging from philosophy to science. Ibn Sina's Philosophy is reported to encapsulate Aristotelian and Neoplatonic influences as well as Muslim theology. The Book of Healing was divided into four different parts; one of which was devoted to mathematics. Interestingly, in this book Ibn Sina divided mathematics into four different branches: geometry, astronomy, arithmetic and music, and then he subdivided each of these branches. The Book of Healing was translated to Latin and it is known by the name *Sanatio*. In addition, Ibn Sina had other 'big hits' in philosophy such as *al-Najat* and *Isharat*.

Besides philosophy and medicine, Ibn Sina contributed to a wide variety of other fields. In Physics, he had some observations regarding the different forms of energy, heat, light and mechan-

ics. Moreover, he wrote about an inter-connection between time and motion. Ibn Sina also contributed to Astronomy. He made several astronomical observations. For example, he observed and suggested that Venus is closer to Earth than the Sun. In the same field, he invented an instrument for observing the coordinates of a star. In addition, Ibn Sina wrote numerous short poems and made some contributions to Chemistry and Music.

The modern scientific advances have been achieved as a result of contributions from different scientists belonging to different nations, and among these great scientists stands proudly and deservedly the name of Ibn Sina, Avicenna, mostly due to his contributions to medicine.

Additional Resources

<http://www.muslimphilosophy.com/sina>

http://www.ummah.net/history/scholars/ibn_sina

<http://www-groups.dcs.st-and.ac.uk/~history/Mathematicians/Avicenna.html>

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communicate information. The concept is well depicted by Wikipedia which is growing at a fast pace and gaining much more interest. GNU and Linux have started the battle a long time before [4] and their success is now imminent. I will not cite its benefits herein (refer to Forum discussion) but I would like to put a particular emphasis on the fact that developing countries could profit from this scheme substantially.

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[1] Editorial. IBScientific 1 (1).

[2] Nature Published online: 14 December 2005. Wiki's wild world".

[3] Nature: 15 December 2005. Special report : "Internet encyclopaedias go head to head".

[4] S. Djerfi (2005). Open Source Software: A Paradigm Shift. IBScientific 1 (2).

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